Breast Development & Physiology

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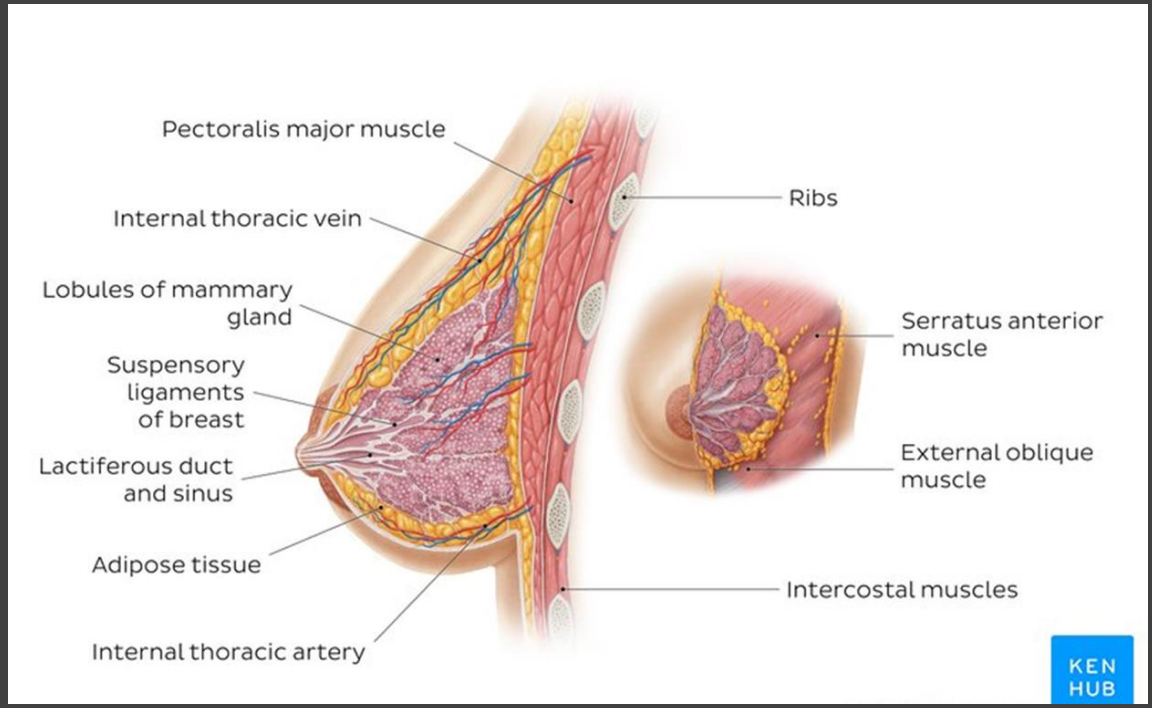
Part 1: Breast Development

Introduction

- The mammary gland is an organ of ectodermal origin, typical of mammalians, whose structure reflects its special function: the production of milk for lactation.
- In human beings the breast has an undoubted aesthetic value
- The size and shape of women's breasts vary considerably. Some women have a large amount of breast tissue and have larger breasts. Others have a smaller amount of tissue with little breast fat.
- A woman's breasts are rarely the same size; usually one breast is slightly larger or smaller, higher or lower or of different shape to the other

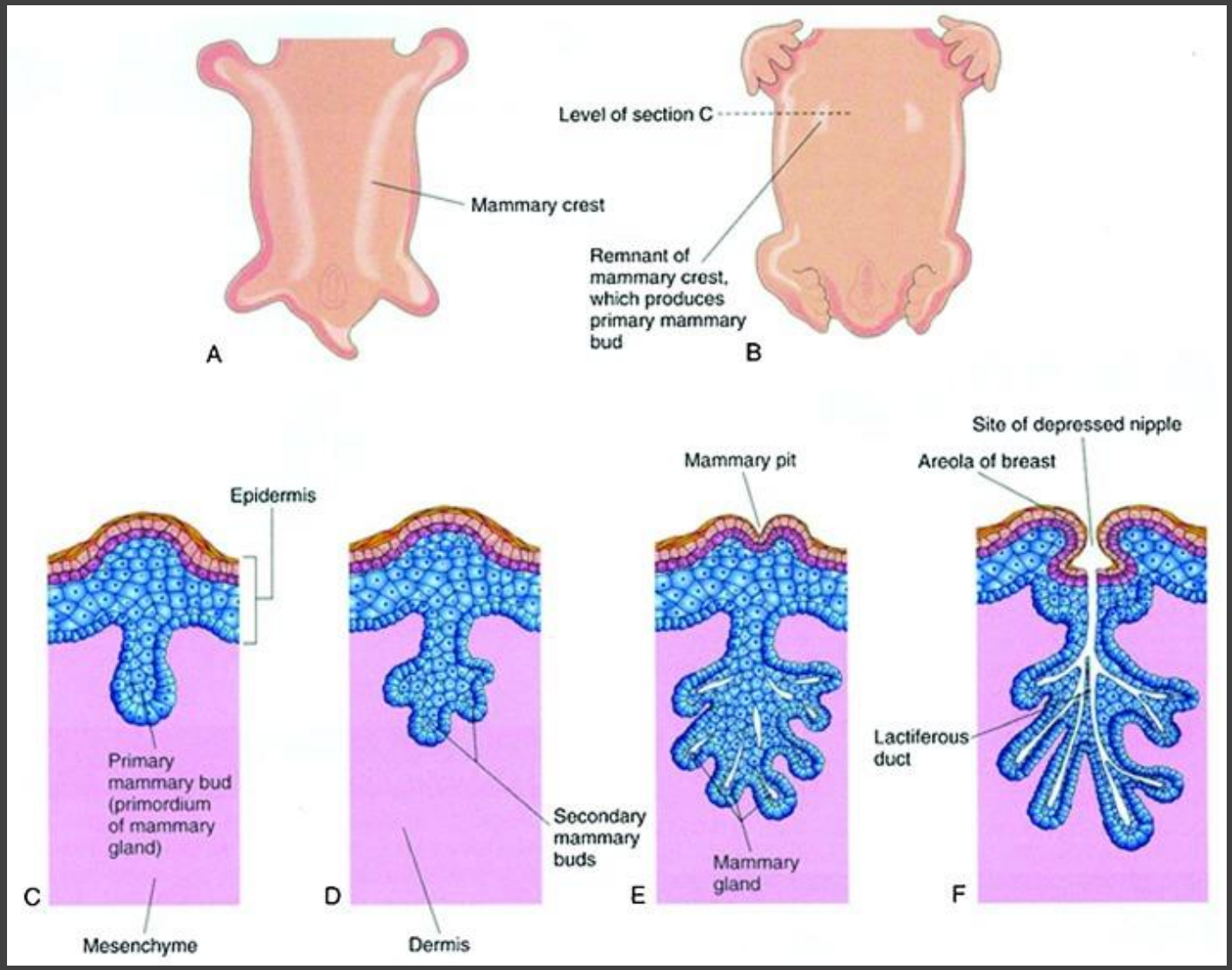
- The inner structure of the mammary gland is made of epithelial components that consist of lobules, where milk is made, which connect to ducts that lead out to the nipple. These lobules and ducts are located and spread throughout the background fibrous tissue and adipose tissue that form the main mass of the breast.

- The structure of the male breast is almost identical to that of the female breast, except that the male breast tissue lacks the specialized lobules because there is no physiologic need for milk production



Breast Development

- The human breast consists of parenchymal and stromal elements.
- The parenchyma forms a system of branching ducts eventually leading to secretory acini development.
- The stroma consists mainly of adipose tissue, providing the environment for development of the parenchyma.
- The process of development of the ductal system and acini is termed branching morphogenesis and although it commences in the fetus, it halts in early childhood until puberty when hormonal stimulation triggers further differentiation.
- Under the influence of hormones, complex reciprocal interactions between the epithelium and mesenchyme lead to differentiation of the prenatally developed rudimentary structure to form a mature mammary gland



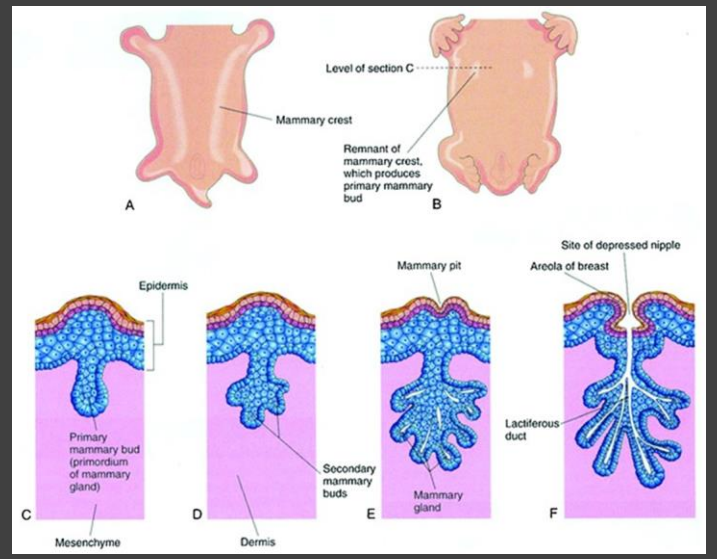
Development of the mammary gland. (**A**) Ventral view of an embryo at 28-days gestation showing mammary crests. (**B**) Similar view at 6-week gestation showing the remains of the mammary crests. (**C**) Transverse section of a mammary crest at the site of the developing mammary gland. (**D–F**) Similar sections showing successive stages of breast development between the 12th week of gestation and birth

A) Prenatal development

- Prenatal breast development can be classified into two main processes; formation of a primary mammary bud and development of a rudimentary mammary gland.
- The earliest stages of embryogenesis are largely hormone independent.
- Hormones and regulatory factors are important for development in the second trimester

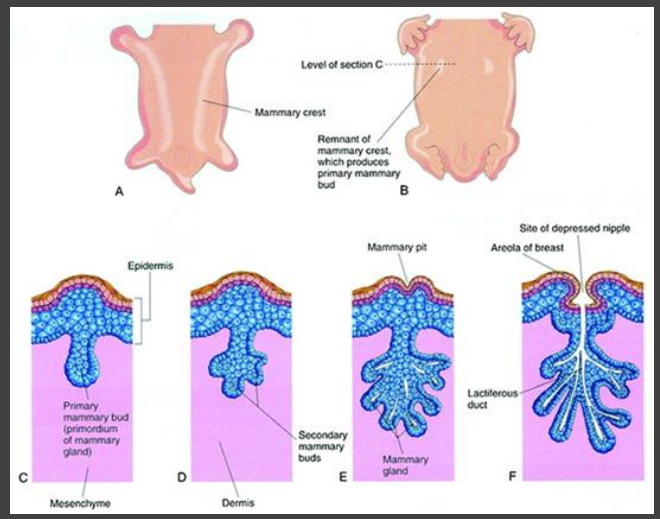
Prenatal development (1st trimester)

- 4 to 6 weeks of gestation, mammary-specific progenitor cells may be seen
- Day 35 of gestation, proliferation of paired areas of epithelial cells in the epidermis of the thoracic region occurs (mammary crest or milk lines)
- Most of the mammary crest atrophies except for paired solid epithelial masses in the pectoral region at the fourth intercostal space
- Toward the end of the first trimester, the primary mammary buds begin to grow downwards into the underlying mesenchyme, under an inductive influence of regulatory factors secreted by the mesenchyme



Prenatal development (2nd trimester)

- Secondary epithelial buds appear from the indentations on the main mammary bud
- Each secondary epithelial bud grows vertically into the mesenchyme surrounding the primary bud and has a slender stalk and bulbous end
- The secondary epithelial sprouts canalize and coalesce forming secondary buds that give rise to lactiferous ducts
- The epithelial cells lining the lactiferous ducts are arranged in two layers, with the layer adjacent to the lumen gaining secretory function while the basal layer differentiates into myoepithelial cells
- By 6 months of gestational age, the basic framework of the gland is established, This is around the time breast tissue in both boys and girls can be apparent



Prenatal development (3rd trimester)

- Repeated branching of the secondary epithelial buds and canalization occur
- The epidermis in the region of the future nipple becomes depressed, forming the mammary pit
- The lactiferous ducts drain into retroareolar ampullae that converge into this pit on the overlying skin.
- The nipple is further delineated by proliferation of the mesoderm (created with smooth muscle fibers)
- The surrounding areola is formed by the ectoderm during the fifth month of gestation.
- During the final weeks of gestation, the loose fibroconnective tissue stroma increases in vascularity
- At term, approximately 15 to 20 lobes of glandular tissue have formed, each containing a lactiferous duct that opens onto the breast surface through the mammary pit.
- Both the surrounding skin and the fibrous suspensory ligaments of Cooper that anchor the breast to the pectoralis major fascia provide support to the breast.

1st Trimester	❑ 4 to 6 weeks of gestation, mammary-specific progenitor cells may be seen ❑ Day 35 of gestation, proliferation of paired areas of epithelial cells in the epidermis of the thoracic region occurs (mammary crest or milk lines) ❑ Most of the mammary crest atrophies except for paired solid epithelial masses in the pectoral region at the fourth intercostal space ❑ Toward the end of the first trimester, the primary mammary buds begin to grow downwards into the underlying mesenchyme, under an inductive influence of regulatory factors secreted by the mesenchyme
2nd Trimester	❑ Secondary epithelial buds appear from the indentations on the main mammary bud ❑ Each secondary epithelial bud grows vertically into the mesenchyme surrounding the primary bud and has a slender stalk and bulbous end ❑ The secondary epithelial sprouts canalize and coalesce forming secondary buds that give rise to lactiferous ducts ❑ The epithelial cells lining the lactiferous ducts are arranged in two layers, with the layer adjacent to the lumen gaining secretory function while the basal layer differentiates into myoepithelial cells ❑ By 6 months of gestational age, the basic framework of the gland is established, This is around the time breast tissue in both boys and girls can be apparent
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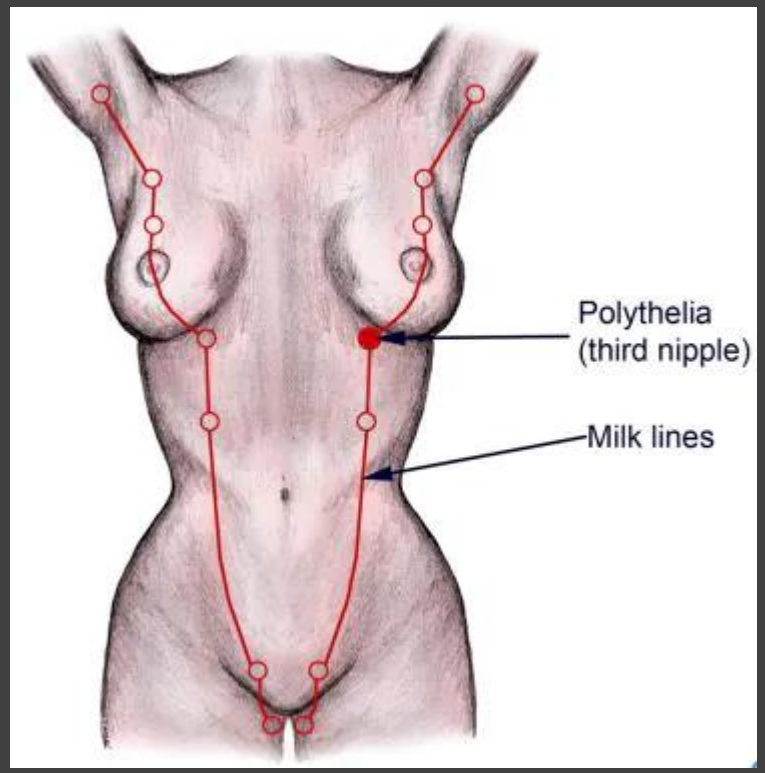
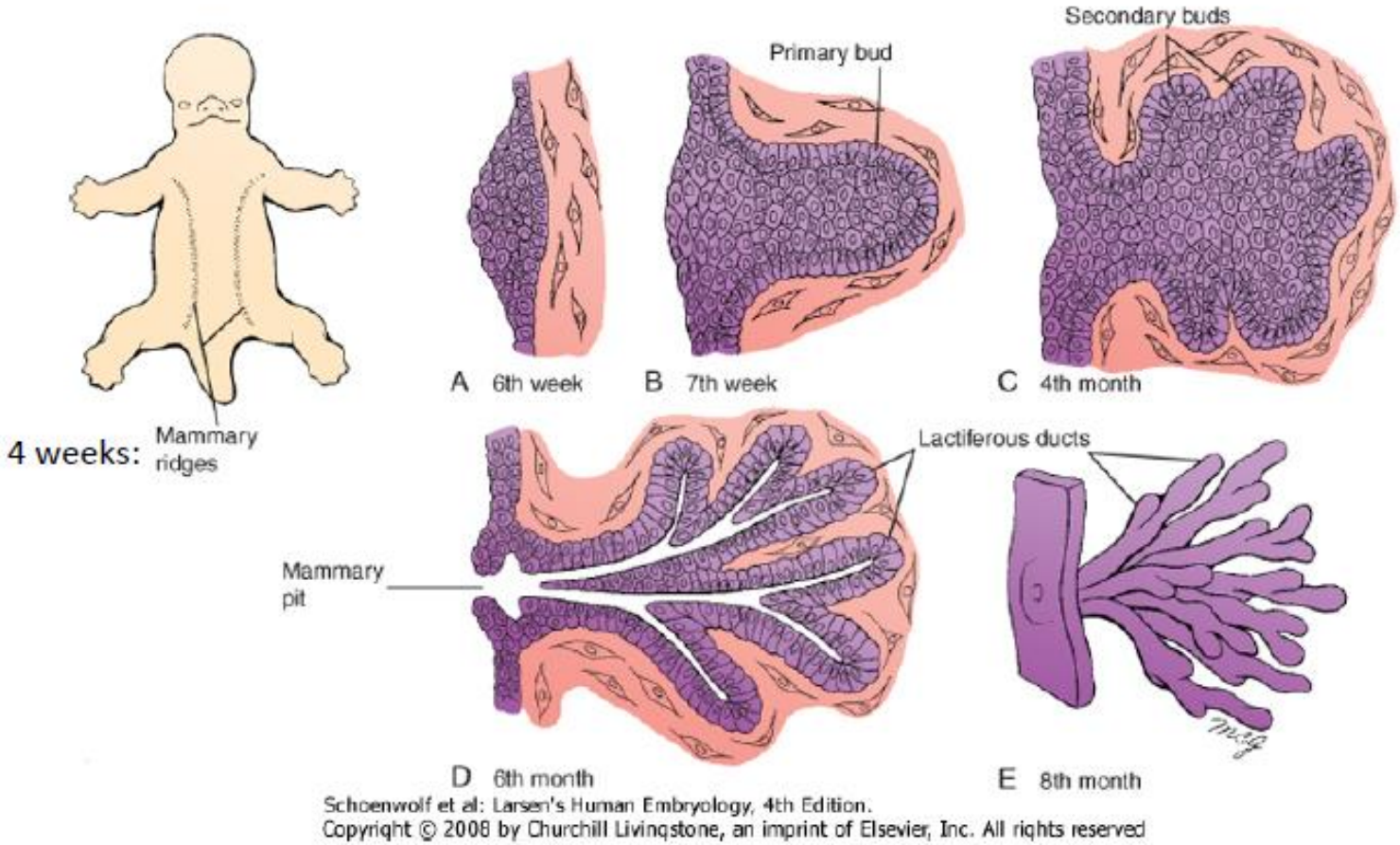


Mammary gland development

Epidermal appendage



Developmental abnormalities

- Accessory nipples (polythelia), are not uncommon along the milk line and are most often found on the chest wall below the breast. These form due to a failure of the regression of the milk streak.

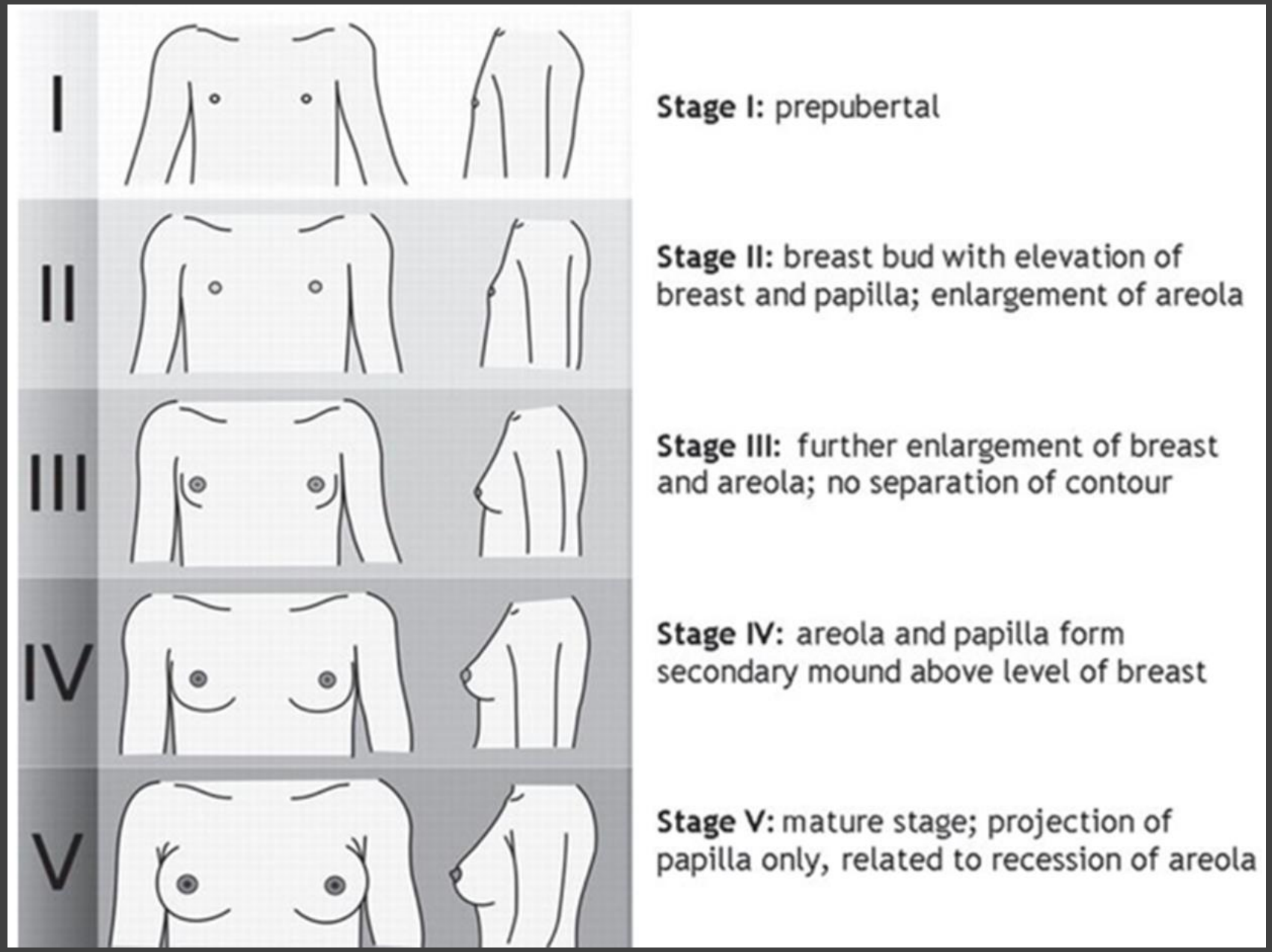
- Inverted nipples are not uncommon, and they are caused by a failure of the evagination of the small mammary pit at birth.

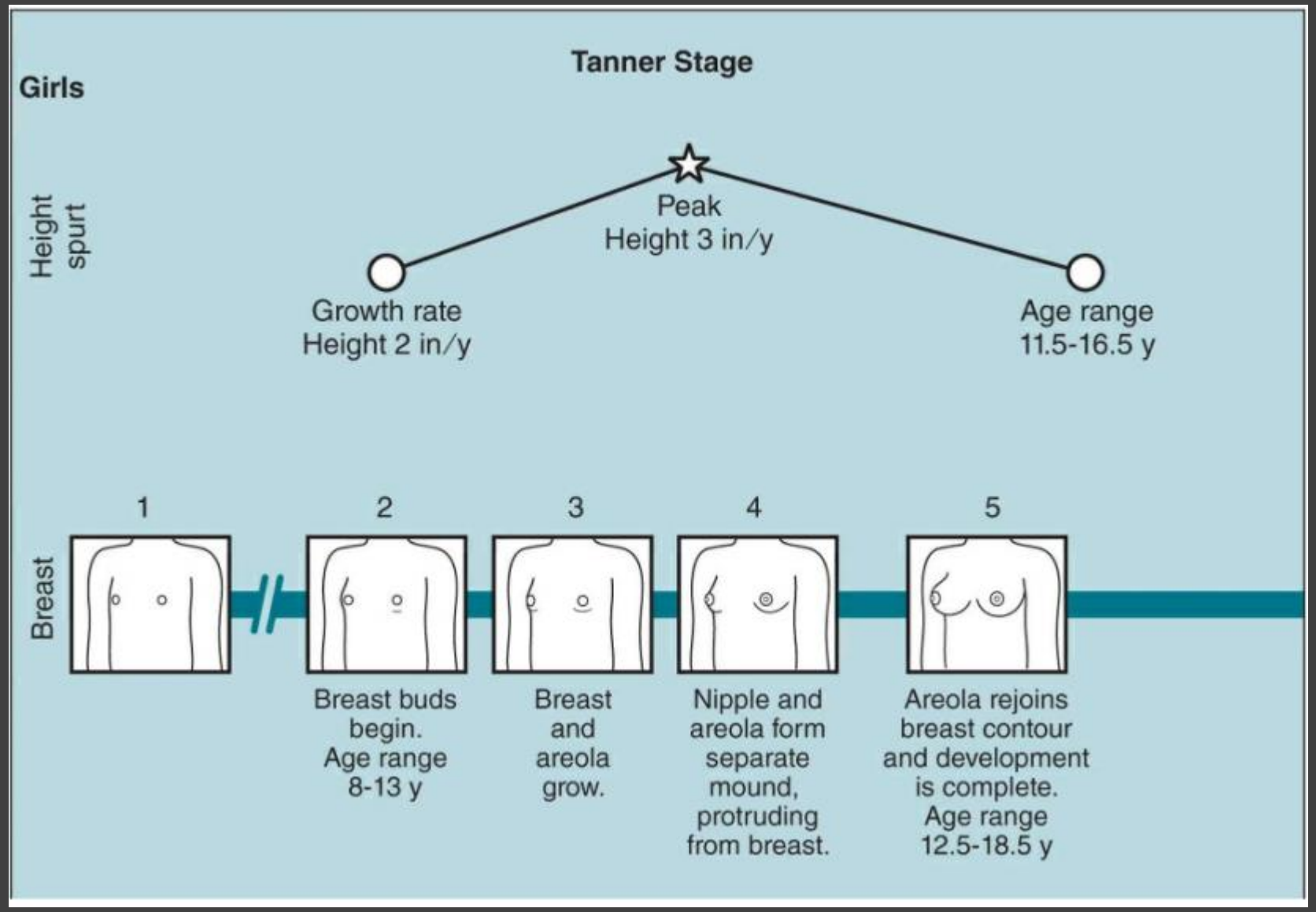
- Accessory mammary glands (polymastia), also due to a failure of the milk line to completely atrophy, are usually found in the axilla and cause the patient to complain of a mass or pain in this area.

- Absence of the breast (amastia) is a rare congenital anomaly; it occurs as a result of an arrested mammary ridge at about the 6th week of gestation.

B) Development of the breast from birth until puberty

- During this period the breast consists of lactiferous ducts, with no alveoli.
- As puberty begins, the circulating estrogen causes the ductal epithelium and surrounding stroma to grow. These ducts begin to branch repeatedly and form collecting ducts and terminal duct lobular units. These ultimately form buds that precede further breast lobules
- vascularity increases and connective tissue increases in volume and elasticity, replacing adipose tissue and providing support for the development of ducts.
- Breast budding is one of the first sign of adolescence in girls, beginning anywhere between age 8 and 13 years.


I
II
III
IV
V
Stage I: prepubertal
Stage II: breast bud with elevation of breast and papilla; enlargement of areola
Stage III: further enlargement of breast and areola; no separation of contour
Stage IV: areola and papilla form secondary mound above level of breast
Stage V: mature stage; projection of papilla only, related to recession of areola


Girls
Tanner Stage
Height spurt
Peak
Height 3 in/y
Growth rate
Height 2 in/y
Age range
11.5-16.5 y
Breast
1
2
3
4
5
Breast buds begin. Age range 8-13 y
Breast and areola grow.
Nipple and areola form separate mound, protruding from breast.
Areola rejoins breast contour and development is complete. Age range 12.5-18.5 y

Development of the breast during pregnancy

- During pregnancy the breast attains its maximum development.
- Secreting alveoli appear, and there is marked growth of the ducts, lobules and alveoli under the influence of luteal and placental sex steroids and prolactin.

1st trimester:

- 1st few weeks → Ductal sprouting and lobular proliferation (i.e. estrogen influence)
- 2nd month → Breast enlargement and increase NAC pigmentation; alveoli has lumen and surrounded by secretory cells

2nd trimester:

- Progesterone causes the lobular formation to exceed the ductal sprouting with a notable raise of prolactin levels.
- At this point the alveoli contain colostrum and the breast continues to enlarge

Late Trimester

- The stroma surrounding the lobules diminishes to make room for the hypertrophied lobules and the breast starts secreting colostrum, which is then replaced by true secretion of milk.

- When lactation ceases, the glandular tissue returns to its resting state

Development of the breast during menopause

- Menopause typically occurs when a woman is in her late 40s and early 50s and it is associated with a variety of symptoms related to the loss of estrogen and progesterone.
- The glandular tissue of the breast atrophies, the connective tissue becomes less cellular and the amount of collagen decreases.
- The loss of strength of the connective tissue usually results in an increase in volume and sag to the breast (i.e. variable and incomplete from woman to woman)

Part 2: Breast Physiology

Introduction

- The breast is an organ specialized for milk formation (lactation), including synthesis, secretion and ejection of milk
- The secretory units of the breasts are the alveoli
- A complex network of hormones and growth factors controls the production of milk by these secretory units.
- The fluctuation of these hormones results in important histologic changes in the breast during pregnancy and during the menstrual cycle.

Estrogen:

- The main female hormone responsible for breast development and maintenance.
- Growth of the ductal system and also maturation and prominence of the nipples, resulting in proliferation of the ductal epithelium, myoepithelial cells and surrounding stroma.
- Estrogen is lipid soluble and in a woman's body is made by the ovaries and to a lesser extent by the adrenal glands.
- It is stimulated to act in the presence of other hormones such as hydrocortisone, insulin-like GFs and growth hormones.

Progesterone:

- Released by the ovaries and induces development of the terminal ducts and lobulo-alveolar structures.
- Similar to estrogen, it needs the presence of the other hormones, such as growth hormones and insulin, to respond.
- Both estrogen and progesterone can increase connective tissue and fat in the breast, thereby leading to the rounded form of the fully developed breast

Hormone (others)	Action	Notes
Prolactin	stimulates mammary growth and differentiation and ultimately milk production	❑ Cooperates with estrogen in ductal development ❑ Cooperate with progesterone in lobulo-alveolar development. ❑ Together with cortisol and insulin prolactin helps to differentiate alveolar cells into milk-secreting cells.
Oxytocin	Contraction of myoepithelial cells, which squeezes milk out from the lobules into the lactiferous ducts.	
Lactogenic hormones	Act alongside the actions of glucocorticoids, insulin and thyroxine for milk production	1. Human placental lactogen (hPL) 2. Prolactin 3. oxytocin

Questions?

Reference

Anatomy and physiology of the breast – Chapter 37

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